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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,500	03/29/2002	Nobuo Hanai	249-255	9448

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/26/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/089,500	HANAI ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,15,16,22-24,32,36,37,40,41,48,50,51,57,58 and 62-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *48* is/are allowed.

6)☒ Claim(s) *1,15,16,24,36,37,50,51,57,63,64 and 66-69* is/are rejected.

7)☒ Claim(s) *22,23,32,40,41,58,62 and 65* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 2-14, 17-21, 25-31, 33-35, 38-39, 42-47, 49, 52-56 and 59-61 have been cancelled.

Claims 1, 22, 32, 36-37, 41 and 65 have been amended.

Claims 66-69 have been added.

2. Claims 1, 15-16, 22-24, 32, 36-37, 40-41, 48, 50-51, 57-58 and 62-69 are pending and under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This Office Action contains New Grounds of Rejections.

Objections/Rejections Withdrawn

5. The objection to the specification as disclosing that the anti-GD3 CDR grafted antibody (i.e., KM8871) fused to hIL-2 is produced by the transformant FERM BP-6790 and also by the transformant deposited as FERM BP-6791 is withdrawn in view of the amendment to the specification filed 11/6/2006.

6. The objection to the specification for improper arrangement is withdrawn in view of applicants' remarks.

7. The objection to the specification in the use of the trademark Super Script™ is withdrawn in view of the amendment to the specification filed 11/6/2006.

8. The objection to claim 22 in the recitation "the H chain V region having the amino acid sequences represented by SEQ ID NO:9", which is gramatically incorrect is withdrawn in view of the amendment to the claim.

9. The objection to claim 65 as containing a hyphen before the term "humanized" is withdrawn in view of the amendment to the claim.

10. The rejection of claim 32 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation of "derivative" is withdrawn in view of the amendment to the claim.

11. The rejection of claim 32 under 35 U.S.C. 112, second paragraph, for lack of antecedent basis for the limitation "The derivative" is withdrawn in view of the amendment to the claim.

12. The rejection of claims 1, 15-16, 23-24, 36-37, 40, 50-51, 58, 62 and 63-64 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation that the claimed humanized antibody comprises the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and the heavy chain variable region of SEQ ID NO:9 or the light chain variable region of SEQ ID NO:54 is withdrawn in view of the amendments to the claims.

13. The rejection of claim 41 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation "the H chain V region having the amino acid sequence represented by SEQ ID NO:53" is withdrawn in view of the amendments to the claim.

14. The rejection of Claims 1, 15-16, 22-24 and 32 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation "a protein or a low molecular weight agent" in claim 1 is withdrawn in view of the amendments to the claims.

15. The rejection of claims 1, 15-16, 24, 36-37, 50-51 and 63-64 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as introducing new matter into the claims is withdrawn in view of the amendments to the claims.

New Grounds of Rejections

16. Claim 69 is rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is unclear if a cell line, which produces an antibody having the exact chemical identity of antibody KM-8871-hIL-2 is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is required. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. (Fundamental Immunology, 242 (William E. Paul, M.D. ed., 3rd ed., 1993, cited on PTO-892 mailed 1/13/05). Therefore, it would require undue experimentation to reproduce the claimed antibody species KM-8871-hIL-2.

The specification lacks complete deposit information for the deposit of anti-GD3 antibody KM-8871-hIL-2. It is unclear whether antibodies possessing the identical properties of antibody KM-8871-hIL-2 are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a cell line is an unpredictable event. Although applicant has provided a written description of a method for producing and selecting cell lines and monoclonal antibodies produced therefrom, this method will not necessarily reproduce the transformant KM8871hIL2 and antibodies, which are chemically and structurally identical to those claimed. It is unclear that one of skill in the art could derive a transformant and antibodies identical to those claimed (KM8871-hIL-2). Undue experimentation would be required to screen all of the possible antibody and cell line species to obtain the claimed transformant KM8871hIL2 and antibody (KM8871-hIL-2).

Applicant's referral to the deposit of transformant KM8871hIL2 as FERM BP-6791 on page 104, lines 21-25 of the specification is an insufficient assurance that the required deposit has been made and all the conditions of 37 CFR 1.801-1.809 met.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed transformant and antibody KM8871-hIL-2, a suitable deposit is required for patent purposes, evidence of public availability of the claimed antibody or evidence of the reproducibility without undue experimentation of the claimed antibody, is required.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit of transformant KM8871hIL2 producing antibody KM8871-hIL-2 has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit of transformant KM8871hIL2 producing antibody KM8871-hIL-2 is not made under the provisions of the Budapest Treaty, then in order to certify that the deposit complies with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance

may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:
(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:
(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and
(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. Alternatively, as an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

The examiner notes that the following rejections were originally set forth in the Office Action mailed 1/13/2005 and are now being reapplied in view of applicants amendments to the claims, which are again drawn to GD3 specific humanized antibodies and antigen-binding fragments thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8. Applicant was advised that such claims were not free of the prior art of record in the previous Office Action mailed 5/4/2006 (see pg. 10, last 4 lines).

17. Claims 1, 15-16, 24, 36-37, 50-51, 57, 63-64 and 66-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shitara et al [a] (U.S. Patent 5,750,078, issued 5/12/1998, cited on PTO-892 mailed 1/13/05) in view of Queen et al (U.S. Patent 5,530,101, issued 6/25/1996, cited on PTO-892 mailed 1/13/05) and Nakamura et al (Cancer, 80(12 Suppl):2650-2655, 15 December 1997, cited on PTO-892 mailed 1/13/05).

The claims are being interpreted as being drawn to an antibody conjugate comprising a GD3-specific humanized antibody or antigen-binding fragment thereof conjugated to a therapeutic agent wherein the humanized antibody comprises the heavy chain CDRs of SEQ ID Nos:3, 4 and 5 and the light chain CDRs of SEQ ID Nos:6, 7 and 8 and human framework and constant regions and wherein the antigen-binding fragment is a Fab, Fab', F(ab')2, a scFv, or dsFv and wherein the therapeutic agent is

human IL-2 or is selected from the therapeutic agents recited in claims 66-68. For this rejection, claim 57 as depending from claim 63 is being interpreted as drawn to a humanized antibody fragment that specifically binds to ganglioside GD3 and comprises the heavy chain CDRs of SEQ ID Nos:3, 4 and 5 and the light chain CDRs of SEQ ID Nos:6, 7 and 8.

Shitara et al [a] teach chimeric antibody KM-871 that specifically reacts with GD3 (see Table 1 at column 30) expressed in human tumors (i.e., melanoma) and KM-871 comprises the constant region of human IgG1 linked to the variable regions of the mouse monoclonal antibody KM-641 (SEQ ID Nos:4 and 5, see columns 37-40), which comprises the claimed heavy chain CDR sequences (SEQ ID Nos:3-5, see residues 31-35, 50-66 and 99-108 of SEQ ID NO:4 at columns 37-38) and light chain CDR sequences (SEQ ID Nos:6-8, see residues 24-34, 50-56 and 89-97 of SEQ ID NO:5 at columns 39-40). Shitara et al [a] do not specifically teach a humanized GD3-specific antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3, 4 and 5 and the light chain CDRs of SEQ ID Nos:6, 7 and 8 and wherein the humanized antibody is conjugated to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2. These deficiencies are made up for in the teachings of Queen et al and Nakamura et al

Queen et al teach chimeric and humanized antibodies for human therapy as well as antibody fragments including Fv, Fab, F(ab)2 and single-chain antibodies (scFv) (see entire document, particularly columns 11-16). Queen et al teach that humanized antibodies are less immunogenic in human patients as compared to mouse and

chimeric antibodies (i.e., reduced human anti-mouse antibody (HAMA) response) and thus, overcome one of the limitations associated with mouse and chimeric antibodies for human therapy (see column 1 and column 16, lines 6-26). Queen et al also teach conjugating the antibodies to cytotoxic agents, radionuclides, chemotherapeutic drugs and cytotoxic proteins for treatment of cancerous cells (see column 19, line 45 to column 20, line 22).

Nakamura et al teach an I^{125} labeled antibody-human IL-2 (hIL-2) immunoconjugate that specifically enhances tumor vascular permeability whereas pretreatment with IL-2 was not tumor specific (see page 2651, left column, Figure 2 and page 2655).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for

therapeutic benefit in human cancer patients in view of Shitara et al [a] and Queen et al and Nakamura et al because Shitara et al [a] teach a chimeric anti-GD3 antibody (KM-871) comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and Queen et al teach humanized antibodies for human therapy, which are less immunogenic in human patients as compared to mouse and chimeric antibodies (i.e., reduced HAMA response) and thus, overcome one of the limitations associated with administering mouse and chimeric antibodies for human therapy as well as conjugating the antibodies to cytotoxic agents, radionuclides, chemotherapeutic drugs and cytotoxic proteins for treatment of cancerous cells and Nakamura et al teach an I^{125} labeled antibody-hIL-2 immunoconjugate specifically enhances tumor vascular permeability whereas pretreatment with IL-2 was not tumor specific. Therefore, one of ordinary skill in the art would have been motivated at the time the invention was made to reduce the immunogenicity of the chimeric GD3-specific antibody of Shitara et al [a] for tumor therapy in human patients and produce a humanized GD3-specific antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 as taught by Shitara et al [a] and one of ordinary skill in the art would have been motivated to conjugate the humanized GD3-specific antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug and hIL-2 for increased therapeutic benefit of human tumors. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the claimed invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ

ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients in view of Shitara et al [a] and Queen et al and Nakamura et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

18. Claims 1, 15-16, 24, 36-37, 50-51, 57, 63-64 and 66-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shitara et al [b] (U.S. Patent 6,437,098 B1, priority to 9/17/1992, cited on PTO-892 mailed 1/13/05) in view of Queen et al (U.S. Patent 5,530,101, issued 6/25/1996, cited on PTO-892 mailed 1/13/05) and Nakamura et al (Cancer, 80(12 Suppl):2650-2655, 15 December 1997, cited on PTO-892 mailed 1/13/05).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and

reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The claims and their interpretation have been described supra.

Shitara et al [b] teach chimeric antibody KM-871 that specifically reacts with GD3 (see Table 1 at column 30) expressed in human tumors (i.e., melanoma) and KM-871 comprises the constant region of human IgG1 linked to the variable regions of the mouse monoclonal antibody KM-641 (SEQ ID Nos:4 and 5, see columns 37-40), which comprises the claimed heavy chain CDR sequences (SEQ ID Nos:3-5, see residues 31-35, 50-66 and 99-108 of SEQ ID NO:4 at columns 37-38) and light chain CDR sequences (SEQ ID Nos:6-8, see residues 24-34, 50-56 and 89-97 of SEQ ID NO:5 at columns 39-40). Shitara et al [b] do not specifically teach a humanized GD3-specific antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3, 4 and 5 and the light chain CDRs of SEQ ID Nos:6, 7 and 8 and wherein the humanized antibody is conjugated to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2. These deficiencies are made up for in the teachings of Queen et al and Nakamura et al

Queen et al have been described supra.

Nakamura et al have been described supra.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients in view of Shitara et al [b] and Queen et al and Nakamura et al because Shitara et al [b] teach a chimeric anti-GD3 antibody (KM-871) comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and Queen et al teach humanized antibodies for human therapy, which are less immunogenic in human patients as compared to mouse and chimeric antibodies (i.e., reduced HAMA response) and thus, overcome one of the limitations associated with administering mouse and chimeric antibodies for human therapy as well as the antibodies conjugated to cytotoxic agents, radionuclides, chemotherapeutic drugs and cytotoxic proteins for treatment of cancerous cells and Nakamura et al teach

an I^{125} labeled antibody-hIL-2 immunoconjugate specifically enhances tumor vascular permeability whereas pretreatment with IL-2 was not tumor specific. Therefore, one of ordinary skill in the art would have been motivated at the time the invention was made to reduce the immunogenicity of the chimeric GD3-specific antibody of Shitara et al [b] for tumor therapy in human patients and produce a humanized GD3-specific antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 as taught by Shitara et al [b] and one of ordinary skill in the art would have been motivated to conjugate the humanized GD3-specific antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug and hIL-2 for increased therapeutic benefit of human tumors. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the claimed invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the CDRs from the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients in view of Shitara et al [b] and Queen et al and Nakamura et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

19. Claims 1, 15-16, 24, 36-37, 50-51, 57, 63-64 and 66-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shitara et al [c] (EP 0533199 A2, published

3/24/1993, cited on PTO-892 mailed 1/13/05) in view of Queen et al (U.S. Patent 5,530,101, issued 6/25/1996, cited on PTO-892 mailed 1/13/05) and Nakamura et al (Cancer, 80(12 Suppl):2650-2655, 15 December 1997, cited on PTO-892 mailed 1/13/05).

The claims and their interpretation have been described supra.

Shitara et al [c] teach chimeric antibody KM-871 that specifically reacts with GD3 (see Table 1 at page 22) expressed in human tumors (i.e., melanoma) and KM-871 comprises the constant region of human IgG1 linked to the variable regions of the mouse monoclonal antibody KM-641 (SEQ ID Nos:4 and 5, see pages 29-30), which comprises the claimed heavy chain CDR sequences (SEQ ID Nos:3-5, see residues 31-35, 50-66 and 99-108 of SEQ ID NO:4 at page 29) and light chain CDR sequences (SEQ ID Nos:6-8, see residues 24-34, 50-56 and 89-97 of SEQ ID NO:5 at page 30). Shitara et al [c] do not specifically teach a humanized GD3-specific antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3, 4 and 5 and the light chain CDRs of SEQ ID Nos:6, 7 and 8 and wherein the humanized antibody is conjugated to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2. These deficiencies are made up for in the teachings of Queen et al and Nakamura et al.

Queen et al have been described supra.

Nakamura et al have been described supra.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a humanized anti-GD3 antibody

or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients in view of Shitara et al [c] and Queen et al and Nakamura et al because Shitara et al [c] teach a chimeric anti-GD3 antibody (KM-871) comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and Queen et al teach humanized antibodies for human therapy, which are less immunogenic in human patients as compared to mouse and chimeric antibodies (i.e., reduced HAMA response) and thus, overcome one of the limitations associated with administering mouse and chimeric antibodies for human therapy as well as the antibodies conjugated to cytotoxic agents, radionuclides, chemotherapeutic drugs and cytotoxic proteins for treatment of cancerous cells and Nakamura et al teach an I^{125} labeled antibody-hIL-2 immunoconjugate specifically enhances tumor vascular permeability whereas pretreatment with IL-2 was not tumor specific. Therefore, one of ordinary skill in the art would have been motivated at the time the invention was made

to reduce the immunogenicity of the chimeric GD3-specific antibody of Shitara et al [c] for tumor therapy in human patients and produce a humanized GD3-specific antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 as taught by Shitara et al [c] and one of ordinary skill in the art would have been motivated to conjugate the humanized GD3-specific antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug and hIL-2 for increased therapeutic benefit of human tumors. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the claimed invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the CDRs from the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients in view of Shitara et al [c] and Queen et al and Nakamura et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

20. Claims 1, 15-16, 24, 36-37, 50-51, 57, 63-64 and 66-68 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,437,098 B1 in view of Queen et al (U.S. Patent 5,530,101, issued 6/25/1996, cited on PTO-892 mailed 1/13/05) and Nakamura et al

(Cancer, 80(12 Suppl):2650-2655, 15 December 1997, cited on PTO-892 mailed 1/13/05).

The instant claims and their interpretation have been described supra.

Claims 1-4 of U.S. Patent 6,437,098 B1 are drawn to a chimeric antibody comprising heavy and light chain variable regions of mouse monoclonal antibody KM-641 produced by transformant KM-641 (FERM BP-3116) and the heavy and light chain constant regions of a human antibody, wherein said chimeric antibody binds ganglioside GD3 and wherein the chimeric antibody comprises a heavy chain variable region that has the amino acid sequence of residues 11 to 129 of SEQ ID NO:18 and/or comprises a light chain variable region that has the amino acid sequence of residues 21-127 of SEQ ID NO:19, which comprise the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8. Claims 1-4 of U.S. Patent 6,437,098 B1 do not specifically teach humanized GD3-specific antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3, 4 and 5 and the light chain CDRs of SEQ ID Nos:6, 7 and 8 and wherein the humanized antibody is conjugated to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2. These deficiencies are made up for in the teachings of Queen et al and Nakamura et al.

Queen et al have been described supra.

Nakamura et al have been described supra.

Claims 1, 15-16, 24, 36-37, 50-51, 57, 63-64 and 66-68 in the instant application are obvious variants of claims 1-4 of U.S. Patent 6,437,098 B1 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed

invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients in view of claims 1-4 of U.S. Patent 6,437,098 B1 and Queen et al and Nakamura et al because claims 1-4 of U.S. Patent 6,437,098 B1 teach a chimeric anti-GD3 antibody comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and Queen et al teach humanized antibodies for human therapy, which are less immunogenic in human patients as compared to mouse and chimeric antibodies (i.e., reduced HAMA response) and thus, overcome one of the limitations associated with administering mouse and chimeric antibodies for human therapy as well as the antibodies conjugated to cytotoxic agents, radionuclides, chemotherapeutic drugs and cytotoxic proteins for treatment of cancerous cells and Nakamura et al teach an I^{125} labeled antibody-hIL-2 immunoconjugate specifically enhances tumor vascular permeability whereas

pretreatment with IL-2 was not tumor specific. Therefore, one of ordinary skill in the art would have been motivated at the time the invention was made to reduce the immunogenicity of the chimeric GD3-specific antibody of claims 1-4 of U.S. Patent 6,437,098 B1 for tumor therapy in human patients and produce a humanized GD3-specific antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 according to the teachings of Queen et al and one of ordinary skill in the art would have been motivated to conjugate the humanized GD3-specific antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug and hIL-2 for increased therapeutic benefit in human cancer patients. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the claimed invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients in view of claims 1-4 of U.S. Patent 6,437,098 B1 and Queen et al and Nakamura et al.

Claims 1, 15-16, 24, 36-37, 50-51, 57, 63-64 and 66-68 are directed to an invention not patentably distinct from claims 1-4 of commonly assigned U.S. Patent 6,437,098 B1. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP

§ 2302). Commonly assigned U.S. Patent 6,437,098 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

21. Claims 1, 15-16, 24, 36-37, 50-51, 57, 63-64 and 66-68 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 2 of U.S. Patent No. 5,750,078 in view of Shitara et al [c] (EP 0533199 A2, published 3/24/1993, cited on PTO-892 mailed 1/13/05) and Queen et al (U.S. Patent 5,530,101, issued 6/25/1996, cited on PTO-892 mailed 1/13/05) and Nakamura et al (Cancer, 80(12 Suppl):2650-2655, 15 December 1997, cited on PTO-892 mailed 1/13/05).

The instant claims and their interpretation have been described supra.

Claim 2 of U.S. patent 5,750,078 is drawn to a human chimeric antibody KM-871 produced by a transformant KM-871 (FERM BP-3512), which is reactive with ganglioside GD3. Claim 2 of U.S. Patent 5,750,078 does not specifically teach the variable region sequences of chimeric antibody KM-871 or a humanized GD3-specific antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3, 4 and 5 and the light chain CDRs of SEQ ID Nos:6, 7 and 8 and wherein the humanized antibody is conjugated to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2. These deficiencies are made up for in the teachings of Shitara et al [c] and Queen et al and Nakamura et al.

Shitara et al [c] have been described supra.

Queen et al have been described supra.

Nakamura et al have been described supra.

Claims 1, 15-16, 24, 36-37, 50-51, 57, 63-64 and 66-68 in the instant application are obvious variants of claim 2 of U.S. Patent 5,750,078 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have

produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients in view of claim 2 of U.S. Patent 5,750,078 and Shitara et al [c] and Queen et al and Nakamura et al because claim 2 of U.S. Patent 5,750,078 teaches the chimeric antibody, KM-871, which binds GD3 and Shitara et al [c] teaches the variable region sequences of chimeric antibody KM-871, which comprise the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and Queen et al teach humanized antibodies for human therapy, which are less immunogenic in human patients as compared to mouse and chimeric antibodies (i.e., reduced HAMA response) and thus, overcome one of the limitations associated with administering mouse and chimeric antibodies for human therapy as well as the antibodies conjugated to cytotoxic agents, radionuclides, chemotherapeutic drugs and cytotoxic proteins for treatment of cancerous cells and Nakamura et al teach an I^{125} labeled antibody-hIL-2 immunoconjugate specifically enhances tumor vascular permeability whereas pretreatment with IL-2 was not tumor specific. Therefore, one of ordinary skill in the art would have been motivated at the time the invention was made to reduce the immunogenicity of the chimeric GD3-specific antibody of claim 2 of U.S. Patent 5,750,078 for tumor therapy in human patients and produce a humanized GD3-specific antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 according to the

teachings of Queen et al and one of ordinary skill in the art would have been motivated to conjugate the humanized GD3-specific antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug and hIL-2 for increased therapeutic benefit of human tumors. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the claimed invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the CDRs from the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients in view of claim 2 of U.S. Patent 6,437,098 B1 and Shitara et al [c] and Queen et al and Nakamura et al.

Claims 1, 15-16, 24, 36-37, 50-51, 57, 63-64 and 66-68 are directed to an invention not patentably distinct from claim 2 of commonly assigned U.S. Patent 5,750,078. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent 5,750,078, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were

commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

22. Claims 1, 15-16, 24, 36-37, 50-51, 57, 63-64 and 66-68 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,495,666 B2 in view of Shitara et al [c] (EP 0533199 A2, published 3/24/1993, cited on PTO-892 mailed 1/13/05) and Queen et al (U.S. Patent 5,530,101, issued 6/25/1996, cited on PTO-892 mailed 1/13/05) and Nakamura et al (Cancer, 80(12 Suppl):2650-2655, 15 December 1997, cited on PTO-892 mailed 1/13/05).

The instant claims and their interpretation have been described supra.

Claims 1-2 of U.S. patent 6,495,666 B2 are drawn to a polypeptide comprising the amino acid sequence of residues 11 to 129 of SEQ ID NO:18 and a polypeptide comprising the amino acid sequence of residues 21-127 of SEQ ID NO:19, which as evidenced by the disclosure of U.S. Patent 6,495,666 B2 these polypeptides are defined as the VH and VL regions of KM-641, which is a monoclonal antibody that binds GD3. Claims 1-2 of U.S. Patent 6,495,666 B2 do not specifically teach a humanized GD3-specific antibody or antigen-binding fragment thereof comprising the heavy chain CDRs

of SEQ ID Nos:3, 4 and 5 and the light chain CDRs of SEQ ID Nos:6, 7 and 8 and wherein the humanized antibody is conjugated to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2. These deficiencies are made up for in the teachings of Shitara et al [c] and Queen et al and Nakamura et al.

Shitara et al [c] have been described supra.

Queen et al have been described supra.

Nakamura et al have been described supra.

Claims 1, 15-16, 24, 36-37, 50-51, 57, 63-64 and 66-68 in the instant application are obvious variants of claims 1-2 of U.S. patent 6,495,666 B2 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients in view of claims 1-2 of U.S. patent

6,495,666 B2 and Shitara et al [c] and Queen et al and Nakamura et al because claims 1-2 of U.S. patent 6,495,666 B2 teach polypeptides comprising residues 11 to 129 of SEQ ID NO:18 and residues 21-127 of SEQ ID NO:19, which are identical to the VH and VL regions of the GD3-specific chimeric antibody KM-871 taught by Shitara et al [c], and which comprises the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and Queen et al teach humanized antibodies for human therapy, which are less immunogenic in human patients as compared to mouse and chimeric antibodies (i.e., reduced HAMA response) and thus, overcome one of the limitations associated with administering mouse and chimeric antibodies for human therapy as well as the antibodies conjugated to cytotoxic agents, radionuclides, chemotherapeutic drugs and cytotoxic proteins for treatment of cancerous cells and Nakamura et al teach an I^{125} labeled antibody-hIL-2 immunoconjugate specifically enhances tumor vascular permeability whereas pretreatment with IL-2 was not tumor specific. Therefore, one of ordinary skill in the art would have been motivated at the time the invention was made to reduce the immunogenicity of the chimeric GD3-specific antibody of claims 1-2 of U.S. patent 6,495,666 B2 for cancer therapy in human patients and produce a humanized GD3-specific antibody or antigen-binding fragment thereof comprising the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 according to the teachings of Queen et al and one of ordinary skill in the art would have been motivated to conjugate the humanized GD3-specific antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug and hIL-2 for increased therapeutic benefit in human cancer

patients. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the claimed invention was made to have produced a humanized anti-GD3 antibody or antigen-binding fragment thereof comprising the CDRs from the heavy chain CDRs of SEQ ID Nos:3-5 and the light chain CDRs of SEQ ID Nos:6-8 and conjugated the humanized antibody or antigen-binding fragment thereof to a cytotoxic agent/protein, a radionuclide, a chemotherapeutic drug or hIL-2 for therapeutic benefit in human cancer patients in view of claims 1-2 of U.S. patent 6,495,666 B2 and Shitara et al [c] and Queen et al and Nakamura et al.

Claims 1, 15-16, 24, 36-37, 50-51, 57, 63-64 and 66-68 are directed to an invention not patentably distinct from claims 1-2 of commonly assigned U.S. Patent 6,495,666 B2. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent 6,495,666 B2, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Conclusions

23. Claims 22-23, 32, 40-41, 58, 62 and 65 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

24. Claim 48 is free of the prior art. The prior art does not teach or fairly suggest the humanized anti-GD3 antibody comprising the heavy and light chain variable region sequences recited in the claim.

25. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827